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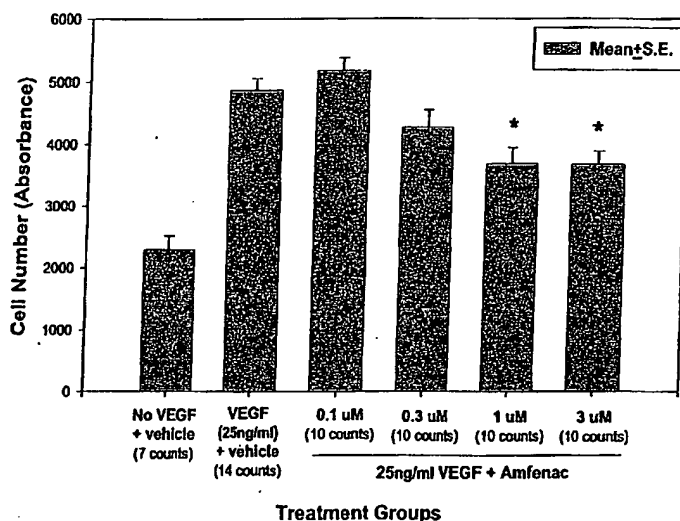
— with international search report

(88) Date of publication of the international search report:
25 March 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD OF TREATING VASCULAR ENDOTHELIAL GROWTH FACTOR MEDIATED VASCULAR DISORDERS USING AMFENAC OR NEPAFENAC

Effect of Amfenac on VEGF-induced cell proliferation
in Bovine Retinal Microvascular Endothelial Cells



[*P < 0.001 vs. VEGF + vehicle (0.1% DMSO)]

(57) Abstract: The use of amfenac and derivatives, including nepafenac, to treat vascular endothelial growth factor mediated vascular disorders.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/11769

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/165 A61K31/196 A61P27/02 A61P27/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, BIOSIS, PAJ, WPI Data, EMBASE, PASCAL, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | US 2002/037929 A1 (GRAFF GUSTAV ET AL) 28 March 2002 (2002-03-28) column 2-3 example 1 claims 1-9 | 1-10 |
| X,P | --- TAKAHASHI KYOICHI ET AL: "Topical nepafenac inhibits ocular neovascularization." INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE. UNITED STATES JAN 2003, vol. 44, no. 1, January 2003 (2003-01), pages 409-415, XP009013970 ISSN: 0146-0404 page 409 page 412-414 --- -/- | 1-10 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

6 October 2003

Date of mailing of the international search report

17/10/2003

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/11769

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X,P | <p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 2002 PENN J S ET AL: "Studies of the Effect and Mechanism of Action of Topical Nepafenac in a Rat Model of ROP." Database accession no. PREV200300154861 XP002247860 abstract & ARVO ANNUAL MEETING ABSTRACT SEARCH AND PROGRAM PLANNER, vol. 2002, 2002, page Abstract No. 2741 Annual Meeting of the Association For Research in Vision and Ophthalmology;Fort Lauderdale, Florida, USA; May 05-10, 2002</p> | 1-10 |
| X,P | <p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 2002 BINGAMAN D P ET AL: "Topical Ocular Delivery of Nepafenac Inhibits Preretinal Neovascularization." Database accession no. PREV200300165352 XP002247861 abstract & ARVO ANNUAL MEETING ABSTRACT SEARCH AND PROGRAM PLANNER, vol. 2002, 2002, page Abstract No. 3920 Annual Meeting of the Association For Research in Vision and Ophthalmology;Fort Lauderdale, Florida, USA; May 05-10, 2002</p> | 1-10 |
| Y | <p>KWAK N ET AL: "VEGF is major stimulator in model of choroidal neovascularization." INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE. UNITED STATES SEP 2000, vol. 41, no. 10, September 2000 (2000-09), pages 3158-3164, XP009013972 ISSN: 0146-0404 page 3161 -page 3162</p> | 1-10 |
| Y | <p>WO 01 15744 A (BRIGHAM & WOMENS HOSPITAL) 8 March 2001 (2001-03-08) page 9 page 3</p> | 1-10 |
| A,P | <p>WO 02 078681 A (ALCON INC ;GRAFF GUSTAV (US); HELLBERG MARK R (US); YANNI JOHN M ()) 10 October 2002 (2002-10-10) page 5 example 2</p> | 1-10 |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1 and 3 refer to vascular diseases defined by reference to a biological mechanism - vascular endothelial growth factor mediated vascular disorders. The claims cover all the conditions mediated by this mechanism, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such conditions. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely for the search term "vascular disorders" and for the diseases mentioned in claims 2 and 4.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/11769

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/11769

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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